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EXAMINER

GABEL, GAILENE

ART UNIT	PAPER NUMBER
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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Application Number: 09/554,956
Filing Date: July 11, 2000
Appelants: BADLEY ET AL.

Marina T. Larson
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed May 24, 2005.

(1) Real Party in Interest

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A statement identifying the real party in interest is contained in the brief.

(2) *Related Appeals and Interferences*

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) *Status of Claims*

The statement of the status of the claims contained in the brief is correct.

(4) *Status of Amendments After Final*

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) *Summary of Invention*

The summary of invention contained in the brief is correct.

(6) *Issues*

The appellant's statement of the issues in the brief is correct.

(7) *Grouping of Claims*

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The rejection of claims 1-3, 5-16, and 22 stand or fall together because appellant's brief does not include a statement that this grouping of claims does not stand or fall together and reasons in support thereof. See 37 CFR 1.192(c)(7).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

5,281,539	SCHRAMM	1-1994
5,082,630	PARTIN et al.	1-1992
6,025,166	PRESTA et al.	2-2000

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

A. Claims 1-3, 7-10, and 12-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Schramm (US Patent 5,281,539).

Schramm et al. disclose a method comprising contacting a first surface upon which a displaceable moiety such as an antibody has been reversibly bound, with a sample, wherein analyte in the sample displaces the reversibly bound moiety causing the displaced moiety to bind to a second surface upon which a capture antibody is bound which produces a signal, and detecting the signal produced by fluorescence or enzyme labels. Schramm et al. teach that the two surfaces can be on separate or same supports that may be in planar, porous, or particulate surface form (see Abstract, especially column 5, line 51 to column 6, line 2, and column 4, line 42 to column 5, line 4). The analyte may be any one of protein hormones (progesterone or testosterone), nucleic acids, peptides (benzoylecgonine), and any other organic or inorganic species of molecules present in a body fluid sample (see column 3, lines 53-59). The first surface comprises intervening molecules including lectins, receptors, membrane proteins, transport proteins, monoclonal antibodies, immunoglobulins (subtype IgG2bk), polyclonal antibodies (bispecific antigen-binding antibodies), complimentary subunits (immunoglobulins), and analyte analogues (other compounds that competitively bind with the analyte) which bind reversibly or loosely to the displaceable moiety (see column 4, lines 48-62 and column 6, line 62 to column 7, line 3). Schramm et al. disclose using electrodes in a sensor to detect modulation of an electrochemical property of the capture moiety wherein modulation is in the form of a detectable signal. If present, analyte continually displaces the displaceable moiety which is then continually captured by the capture antibody so that the measured signal from the sensors continuously

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changes, with the concentration of the analyte captured on the sensor (see column 8, lines 27-62 and Figure 7).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

B. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schramm (US Patent 5,281,539) in view of Partin et al. (US Patent 5,082,630).

Schramm et al. has been discussed supra. Schramm et al. differs from the instant invention in failing to teach that the detectable signal comprises the generation or the modulation of, an evanescent or acoustic wave.

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Partin et al. disclose a fiber optic detector for use in immune testing. In practice, Partin et al. disclose coating a distal end of an optical fiber or waveguide (first surface) with antibody, then saturating the fiber with fluorescent-tagged drug derivative, i.e. antigen (displaceable moiety). Thereafter, the fiber is exposed to an airborne sample of the analyte, i.e. drug, to be detected. If the analyte is present, the analyte molecules displace some of the bound, fluorescent-tagged derivative, resulting in a decrease (modulation) in signal as detected by a detecting diode. The extent of the decrease is proportional to the concentration of drug molecules in the surrounding environment. See column 4, lines 49-64 and column 4.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute a waveguide as taught by Partin, to capture and detect the signal in the form of an evanescent wave generated in the method of Schramm, because Schramm appears to be generic in the type of detection method used, depending on the labels used, and Partin taught that the optical fibers and waveguides for use in detection have the advantage of being sensitive detectors even at extremely low concentrations of analyte.

C. Claim 5, 6, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schramm (US Patent 5,281,539) in view of Presta et al. (US Patent 6,025,166).

Schramm et al. has been discussed supra. Schramm et al. differs from the instant invention in failing to disclose specifically using fusion protein in claim 5 as a displaceable moiety.

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Presta et al. disclose using fusion proteins (chimeric proteins) in competitive displacement assays. Specifically, Presta et al. tested binding specificity of fusion proteins in a cellular environment, wherein the competitive displacement assay was done with iodinated neurotrophins.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute the intervening moiety or the displaceable moiety in the method of Schramm et al., with fusion or chimeric proteins as taught by Presta because Presta specifically taught application of fusion proteins in displacement assays such as in the methods of Schramm et al.

Schramm et al. and Presta are silent in teaching mimitopes as analyte analogues in claim 6 or as an intervening moiety in claim 22.

It would also have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute mimitopes as intervening molecules or analyte analogues in the method of Schramm as modified by Presta, because mimitopes constitute obvious variations of complimentary subunits and analyte analogs taught in the method of Schramm, for use in recognizing specific epitopes in the immunological assay art.

(11) Response to Argument

5. Appellant's arguments filed May 24, 2005 have been fully considered but they are not persuasive.

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A) Appellant argues that Schramm et al. fails to anticipate the claimed invention because Schramm is not enabling as to Figure 7. Appellant specifically contends that the sensors in Schramm's Figure 7 are said to be electrodes, i.e. Clark electrodes, which are oxygen electrodes, and that they would not directly detect anything that would be bound to the sensor surface, nor appear to have anything to do with the device as disclosed by Schramm. Appellant further argues that there is no description of how signal is generated in the system using Clark electrodes, and how the signal depends on the binding of the displaceable moiety to the surface in Sensor 2.

In response, Appellant's argument that Schramm et al. is not enabling is not on point. Specifically, claim 12 of Appellant's claimed invention recites that "capture of the displaceable moiety by the capture moiety" provides a modulation of an electrochemical property of the capture moiety which provides a detectable signal. In support for this claim, Appellant provides in the disclosure at page 8, first full paragraph and page 13, second full paragraph, wherein the capture moiety is an antibody immobilized to an electrically conductive support (electroactive surface), wherein binding of the displaceable moiety to the capture moiety alters an electrochemical property, i.e. redox potential, of the capture moiety, generating a signal which may be detected by amperometric, voltammetric, or coulometric means. Schramm et al. provides use of Clark electrodes (oxygen electrodes) which are electrochemical sensors that inherently have electrically conductive support or surfaces for measuring any change of an electrochemical property, i.e. redox potential, manifested by the displacement of the displacement moiety (conjugate) by analyte and binding of the conjugate to the

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[capture] antibody, wherein a detectable signal is measured by the sensor. Accordingly, Appellant's description of electrochemical application of the method appears to be consonant with the description provided by Schramm et al. at column 8, lines 27-51.

B) Appellant argues that there is no evidence that capture of conjugate 30" at sensor 2 in Schramm's Figure 7 results in the formation of species capable of producing a detectable signal.

In response, a signal in the context of the claimed invention and Schramm et al. is a change from the baseline (background noise) which is always the first signal that provides an indication of binding or capture. Additionally, column 8, lines 27-51 of the Schramm reference which explains Figure 7, provides that the presence of analyte causes a continuous displacement of displaceable moiety from Sensor 1 for capture of the displaceable moiety into Sensor 2, which results to continuous change of concentration of analyte in each individual sensor, and the change in concentration of analyte in each sensor including Sensor 2, is manifested as a measured signal. Hence, the displaceable moiety "species" generated in Sensor 2 is capable of producing its distinct detectable signal separate from that in Sensor 1, and the "[detectable, distinct] signal is not generated unless and until the displacement moiety is captured on the second surface. Additionally at column 5, lines 51-68, Schramm et al. provide that "upon exposure to substrate solution, the enzyme develops color on the membrane support" and "[U]pon being bound at membrane, the conjugate (displaceable moiety) converts the substrate to a colored product (detectable signal)." As each and every

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element and function recited and described by Appellant is consonant with the teaching of Schramm, it is said that Schramm et al. anticipates the claimed invention.

C) Appellant argues that claim 2 is not anticipated, as there is no disclosure of a displaceable moiety that is an immunoglobulin.

In response, claim 2 recites that the displaceable moiety is an immunoglobulin or an antigen-binding derivative thereof. Schramm et al. provide at page 4, lines 48-61 that analyte-binding members or antigen-binding members or derivatives of the analyte include any one of "complimentary subunits (immunoglobulins or antigen-binding derivatives), monoclonal antibodies, polyclonal antibodies, ... and *other compounds that selectively and competitively bind with the analyte*". Accordingly, Schramm et al. appears to anticipate claim 2.

D) Appellant argues that claim 3 is not anticipated, as there is no disclosure of a displaceable moiety that is a bispecific antibody or bispecific antigen-binding derivative thereof.

In response, claim 3 recites that the displaceable moiety is a bispecific antibody or bispecific antigen-binding derivative thereof. Schramm et al. provide at page 4, lines 48-61 that analyte-binding members or antigen-binding members or derivatives of the analyte include any one of "complimentary subunits, monoclonal antibodies, polyclonal antibodies (bispecific antibody or bispecific antigen-binding derivative thereof), ... and

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other compounds that selectively and competitively bind with the analyte". Accordingly, Schramm et al. appears to anticipate claim 3.

E) Appellant argues that claim 8 is not anticipated as there is no disclosure of an analogue of the analyte bound to the first surface (Sensor 1).

In response, claim 8 recites that the intervening molecule is an analogue of the analyte of interest [bound to the first surface]. Schramm et al. provide at page 4, lines 48-61 that [analyte] binding members, i.e. intervening molecules, immobilized on the first and second surfaces include any one of "lectin, receptors, membrane proteins, complimentary subunits, monoclonal antibodies, polyclonal antibodies ... and *other compounds that selectively and competitively bind*", i.e. *analyte analogue, with the analyte*. Accordingly, Schramm et al. appears to anticipate claim 8.

F) Appellant argues that claim 22 is not anticipated, as there is no disclosure of a mimitope of the analyte of interest bound to Sensor 1.

In response, Appellant's argument is not on point as claim 22 is based on an obviousness rejection in view of a secondary reference.

G) Appellant argues that Schramm et al. fails to anticipate the claimed invention because there is nothing in Schramm which shows any modification of an electrochemical property of the capture moiety which is required by claim 12. Appellant

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points out that claim 12 states that capture of the displaceable moiety by the capture moiety directly modulates an electrochemical property of the capture moiety.

In response, claim 12 of Appellant's claimed invention, indeed, states that capture of the displaceable moiety by the capture moiety directly modulates an electrochemical property of the capture moiety which provides a detectable signal. In support for this claim, Appellant provides in the disclosure at page 8, first full paragraph and page 13, second full paragraph, wherein the capture moiety is an antibody immobilized to an electrically conductive support (electroactive surface), wherein binding of the displaceable moiety to the capture moiety alters an electrochemical property, i.e. redox potential, of the capture moiety and wherein signal is generated and detected by amperometric, voltammetric, or coulometric means. Schramm et al. provides use of Clark electrodes (oxygen electrodes) which are electrochemical sensors that inherently have electrically conductive support or surfaces for measuring any change of an electrochemical property, i.e. redox potential, manifested by the displacement of the displacement moiety (conjugate) by analyte and binding of the conjugate to the [capture] antibody, wherein a detectable signal is measured by the sensor. Accordingly, Appellant's description of electrochemical application of the method appears to be consonant with and encompass the description provided by Schramm et al. at column 8, lines 27-51.

H) Appellant argues that the combination of Schramm with Partin is improper and does not render obvious the claimed invention because the relationship of Partin with

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Schramm is unclear. Applicant specifically contends that the Examiner has not indicated where in Partin there is any disclosure of an evanescent or acoustic wave.

In response, Schramm teaches contacting the first surface upon which a displaceable moiety such as an antibody has been reversibly bound, with a sample wherein analyte in the sample displaces the reversibly bound moiety causing the displaced moiety to bind to a second surface upon which a capture antibody is bound and detecting the signal which can be produced by fluorescence or enzyme labels. Partin is incorporated with the teaching of Schramm only for the teaching of a detectable signal generated by an evanescent or acoustic wave wherein if analyte is present in a sample, the analyte molecules displace some of the bound, fluorescent-tagged derivative, resulting in a decrease (modulation) in signal as detected by a detecting diode. The extent of the decrease is proportional to the concentration of the analyte. Partin specifically discloses application of displacement assays that measure modulation of evanescent wave using waveguides at column 2, lines 49-64. All waveguides inherently function in the same way for detecting signal generated by modulation of an evanescent wave. In support for this rebuttal, Examiner points to columns 5-6 of Carter et al. (US Patent 4,608,344) which explains the concept of measuring evanescent wave in waveguides. Accordingly, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to capture and detect the signal generated in the method of Schramm using the waveguide as taught by Partin because Schramm appears is generic in the type of detection method used, depending on the labels used, and Partin taught that the optical fibers and waveguides

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in detection methods have the advantage of being sensitive even at extremely low concentrations of analyte.

I) Appellant argues that Schramm in view of Presta does not render obvious the claimed invention, specifically claims 5, 6, and 22, because Presta fails to remedy the deficiency of Schramm which fails to teach intervening molecules as analogue of the analyte.

In response, Schramm et al. provide at page 4, lines 48-61 that [analyte] binding members, i.e. intervening molecules, immobilized on the first and second surfaces include any one of "lectin, receptors, membrane proteins, complimentary subunits, monoclonal antibodies, polyclonal antibodies ... and *other compounds that selectively and competitively bind*", i.e. *analyte analogue, with the analyte*. Accordingly, Schramm et al. appears to anticipate claim 8 and the combination of Presta thereto which discloses using fusion proteins (chimeric proteins) in competitive displacement assays, renders obvious the claimed invention. It would have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute the intervening moiety or the displaceable moiety in the method of Schramm et al., with fusion or chimeric proteins as taught by Presta because Presta specifically taught application of fusion proteins in displacement assays such as in the methods of Schramm et al. It would also have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute mimitopes as intervening or displaceable moieties in the method of Schramm and Presta, because mimitopes and fusion proteins constitute obvious variations of

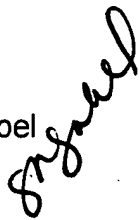
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binding members or analogs for use in recognizing specific epitopes in the immunological assay art.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Gailene R. Gabel
June 27, 2005

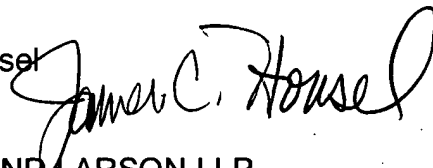


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